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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,840	03/13/2001	Gregory R. Mundy	10274-034001	4957

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,840	MUNDY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,9,31,32,40 and 42-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,9,31,32,40 and 42-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/7/06 has been entered.

2. Claims 1-2, 4-5, 9, 31-32, 40 and 42-48 are pending an under examination in the instant application.

3. Applicant's IDS, filed 4/7/06, is acknowledged.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-2, 4-5, 9, 31-32, 40 and 42-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,692,742 (IDS Ref. No. AD) in view of Masellis-Smith et al (IDS Ref No. AJ OR Lokhorst et al (Blood 84:2269-2277, 1994 of record).

The US `742 patent teaches teach and claims a method for treating multiple myeloma patients comprising administering anti-IL-6 antibodies (a reshaped human PM-1 antibody with melphalan to a subject in need of such treatment) (see patented claim 1in particular), wherein the reshaped human PM-1 antibody is the antibody hPM-1(see patented claim 2 in particular) The `742 patent further teaches that the effective dosage of anti-IL-6 receptor antibody is chosen from the range of 0.001 mg to 1000 mg per kg of body weight per day. Preferably, the dosage is selected from the range of 0.01 to 50 mg per body weight (see col., 15, line 24-28 in particular). The `742 patent teaches that monoclonal antibodies (col., 8, line 2), chimeric antibody and humanized antibody can be used for the purpose of lowering xenogenic antigenicity against humans (see co.,

9, lines 1-6 in particular). Further, the `742 patent teaches that human antibody having the activity of binding to and neutralizing IL-6 receptor (col., 7, lines 33-41 in particular). In addition, the `742 patent teaches that fragments of antibody such as Fab, F(ab')2, Fv or single-chain Fv (scFv) (see col., 10, lines 33-35 in particular). Furthermore, the ` 742 patent teaches compositions comprising a nitrogen mustard anticancer agent and anti-IL-6 receptor antibody (see col., 15, lines 13-15 in particular).

The reference teaching differs from the claimed invention by not expressly disclosing to employ an antibody anti-alpha4 integrin antibody or antigen binding fragment thereof in claim 1, wherein the antibody or antigen binding fragment thereof is an anti-alpha4/beta1in claim 2, wherein the anti-alph4 integrin antibody is an antibody/fragment that antagonizes the interaction of both VLA-4 and alpha4beta 7 with their respective alpha4 ligands, b) and antibody/fragment that antagonizes the interaction of VLA-4 with its alpha4 ligand, and c) an antibody/fragment that antagonizes the interaction of alpha4beta7 with its alpha4 ligand in claim 4.

Masellis-Smith et al teach function-blocking monoclonal antibodies such as mAbs against very late antigen 4 that inhibit the CD19+ multiple myelom blood B cell interaction with BM fibroblasts. Furthermore, Masellis-Smith et al teach that the alpha4beta7 ligand is mediated MM blood B cell adhesion (see the entire document and abstract page 930 in particular).

Lokhorst *et a*l teach monoclonal antibodies directed to the α4-integrin (VLA-4) that inhibit binding of purified myeloma cells to long term bone marrow cultures (LTBMC) from patients with multiple myeloma. Furthermore, the antibodies to VLA-4 inhibited the induced IL-6 secreation. Furthermore, Lokhorst *et al* teach that the intimate cell-cell contact is a prerequisite for IL-6 induction and the physical separation of plasma cells and LTBMC by mechanical means such as monoclaonal antibodies to VLA-4 which is involved in the adhesion process, inhibit the induction of IL-6 production by LTBMC. (entire document and abstract page 2269, and page 2276, left column 2nd paragraph in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti-IL-6 antibody taught by the `742 patent with the antibody that specifically binds the α4 integrin taught by Masellis-Smith *et al* or Lokhorst *et al*., in a method of treating multiple myeloma (MM) taught by the `742 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to to do so because antibodies against alpha4 integrin inhibit cell-cell contact which is a prerequisite for IL-6 induction as taught by Lokhorst *et al* and because antibodies against alpha4 integrin inhibit the adhesion of alpha4beta7 integrin of B cells from MM patients with its ligand on the bone marrow (BM) fibroblast and hence prevent extravasation into the BM.

Claim 9 is included because the claimed dosage of about 0.1 to about 20 mg/kg body weight are within the dose range taught by the `742 patent.

Claim 44 is included because the referenced anti-alpha4 antibodies are B epitope because anti-

alpha4 antibody is an antibody which can bind VLA-4 at a site involved in ligand recognition and block VCAM-1 binding. Thus the referenced anti-alpha4 antibody belongs by definition to the B epitope-specific group. Therefore, being B-epitope-specific is considered an inherent property of the referenced antibody.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 12, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600